

REMARKS

In the April 10, 2008 Advisory Action, the Examiner refused to enter the March 7, 2008 Amendment and Response. The Examiner also commented on the proposed amendment to claim 34. Applicants have considered the Examiner's comment and file this response to respond to both the November 7, 2007 Final Office Action and the April 10, 2008 Advisory Action.

Applicants request reconsideration of the above-identified application in view of the foregoing amendments and following remarks.

The Claim Amendments

Applicants have amended claim 34 to delete the phrase "or a function-conservative fragment thereof".

Applicants have amended claim 35 to recite an "isolated" mutant PAMP, to delete the recitation of mutant PAMP fragments and substantially homologous mutant PAMP fragments, and to incorporate the limitation from claim 36 (now cancelled) that the mutant PAMP is mutated such that the mutation results in changes in A β ₄₂ peptide levels, A β ₄₀ peptide levels, or A β ₄₂/A β ₄₀ peptide ratio. Support for these amendments can be found in, for example, Examples 1 and 2.

Applicants have amended claim 37 to improve its form, to recite an "isolated" mutant human PAMP, and to delete the recitation of mutant PAMP fragments.

Applicants make these amendments and cancellations without waiver of their rights to continue to prosecute and to obtain claims directed to the former subject matter either in this application or in other applications claiming the priority and benefit of this application.

None of the amendments presents new matter.

Claims 34, 35 and 37 remain pending in this application.

The Maintained Rejections

35 U.S.C. § 112, Second Paragraph: Indefiniteness

Claims 34-36 are rejected under 35 U.S.C. 112, second paragraph, for allegedly being indefinite. Each part of the rejection is discussed separately below.

The Examiner states that, in claim 34, no function is assigned to the recited "function conservative fragment" of PAMP. The Examiner states that, while applicants have urged that one skilled in the art would understand such a fragment in light of the specification, the intended function of the fragment is not set forth in the claim. The Examiner further states that "[i]n order for one to determine which fragment of PAMP is intended, an assayable function must be attributed to the fragment."

Applicants traverse. In light of the teachings of the specification, one of ordinary skill in the art would recognize and understand that a function-conservative variant refers to any PAMP variant which retains a function attributed to full-length PAMP. However, solely to expedite prosecution of this application, applicants have amended claim 34 to delete the phrase "or a function-conservative fragment thereof".

With regard to claim 36, the Examiner argues that the biochemical changes similar to those associated with mutations in presenilin-1, presenilin-2 or β -amyloid precursor protein are unclear.

Applicants traverse to the extent that the rejection applies to amended claim 35. In light of the specification, the skilled worker would understand and recognize the metes and bounds of the phrase "biochemical changes similar to those associated with mutations in presenilin-1, presenilin-2 or β -amyloid precursor protein". However, solely to expedite prosecution, applicants have cancelled claim 36 and have amended claim 35 to recite that the mutant PAMP is mutated such that the mutation results in changes in $A\beta_{42}$ peptide levels, $A\beta_{40}$ peptide levels, or $A\beta_{42}/A\beta_{40}$ peptide ratio.

In the context of claim 35, the Examiner argues that a mutant PAMP substantially homologous to human, mouse or *D. melanogaster* PAMP is not clear. According to the Examiner, it is unclear as to whether man-made mutations in human, mouse or *D. melanogaster* PAMP would be considered substantially homologous or if other species of PAMP would be considered mutant PAMPs. The Examiner additionally states that the term "substantially homologous" is indefinite because it is unclear which regions are homologous.

Applicants traverse. Solely to expedite prosecution of this application, however, they have amended claim 35 to delete the recitation of substantially homologous mutant PAMP fragments.

In light of the above arguments and amendments, applicants respectfully request that the Examiner reconsider and withdraw the 35 U.S.C. § 112, second paragraph, rejections.

35 U.S.C. § 102(a)

Claims 35 and 36 stand rejected under 35 U.S.C. 102(a) as allegedly being anticipated by the *C. elegans* Sequencing Consortium ("Consortium"). According to the Examiner, the Consortium teaches an amino acid sequence that shares 99.7% identity to *C. elegans* PAMP (SEQ ID NO: 12) and the instant specification teaches that this homologue is identical to the sequence disclosed by the Consortium. The Examiner states that claims 35 and 36 are anticipated by the Consortium reference "because one PAMP can be considered to be a mutant of the PAMP of another species; thus, the *C. elegans* PAMP is a mutant of the human, mouse, and *Drosophila* PAMP". The Examiner further states that *C. elegans* PAMP is substantially homologous to human, mouse, or *D. melanogaster* PAMP and that it is considered to comprise a functional fragment of the human, mouse, and *Drosophila* PAMP.

Applicants traverse. However, solely to expedite prosecution of this application, applicants have amended claim 35 to delete the recitation of substantially homologous mutant PAMP fragments and have cancelled claim 36, without prejudice.

In light of the amendments and arguments presented above, applicants request that the Examiner reconsider and withdraw the 35 U.S.C. § 102(a) rejection of the pending claims.

New Objections and Rejections

The Objection

The Examiner objects to claim 36 for depending from non-existent Claim 39.

Applicants have cancelled claim 36 without prejudice. Thus, the objection is moot.

35 U.S.C. § 101

Claims 35 and 36 stand rejected under 35 U.S.C. § 101 for allegedly being drawn to non-statutory subject matter because the claimed proteins are not stated to be isolated or purified.

Applicants have amended claim 35 to recite an "isolated" PAMP and have cancelled claim 36 without prejudice thus obviating the Examiner's rejection.

35 U.S.C. § 102(b)

Claims 35-37 stand rejected under 35 U.S.C. § 102(b) as being anticipated by a single amino acid such as alanine. According to the Examiner, because claims 35 and 37 are drawn to a fragment of mutant PAMP without an assigned activity, alanine would qualify as such a fragment.

Applicants have deleted the recitation of mutant PAMP fragments from claims 35 and 37 thus obviating the Examiner's rejection. In addition, applicants have cancelled claim 36 without prejudice. Applicants respectfully request that the Examiner withdraw the rejection.

35 U.S.C. § 112, First Paragraph: Written Description

The Examiner has rejected claims 35-37 for allegedly failing to comply with the written description requirement. The Examiner states that because the claims do not correlate

the mutant PAMP fragments with a defined activity, applicants are not in possession of the fragments. Applicants traverse.

However, solely to expedite prosecution, applicants have deleted the recitation of mutant PAMP fragments from claims 35 and 37 and have cancelled claim 36 without prejudice. Thus, the Examiner's rejection is obviated.

The Examiner has rejected claim 34 for allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to the skilled artisan that the applicants were in possession of the invention at the time of filing. The Examiner states that the term "functional conservative fragments" of PAMP is not taught in the specification. The Examiner notes, however, that "functional-conservative variants" are defined on page 15, paragraph 2, of the specification.

Applicants have amended claim 34 to delete the phrase "or a function-conservative fragment thereof" thus obviating the Examiner's rejection.

In light of the amendments and arguments presented above, applicants request that the Examiner reconsider and withdraw the new rejections of the pending claims.

Application No. 10/763,502

Reply to November 7, 2007 Office Action and April 10, 2008 Advisory Action

Response dated May 5, 2008

CONCLUSION

Applicants request favorable consideration of the application and early allowance of the pending claims.

Respectfully submitted,



James F. Haley, Jr. (Reg. No. 27,794)

Attorney for Applicants

Raymond M. Doss (Reg. No. 61,000)

Agent for Applicants

ROPES & GRAY LLP

Customer No. 1473

1211 Avenue of the Americas

New York, New York 10036

Tel.: (212) 596-9000

Fax: (212) 596-9090